On the polylactose nature of chondroitin and keratan sulphates

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The recognition that keratan and chondroitin sulphates are based on the same polylactose backbone simplifies the study of heteroduplex formation between them, suggests insights into structure–function relationships in tissues, and permits new definitions of the linkage regions.

When the repeating units of keratan sulphate (KS) and chondroitin sulphates (CS) are written not with the HexNAc to the right, according to previous convention, but with the D-galacto and D-gluco rings aligned, their polymer backbones are seen to be identical, consisting of identical disaccharides linked identically (Scott, 1991). In this note some consequences are briefly discussed, leading to simpler definitions of the linkage region versus the polymer chain, and to new questions about relationships

Figure 1 Primary, secondary and tertiary structures involving CS and KS

I and II, structures of KS and CS respectively. Mainly on the basis of endo-hexosaminidase degradation, which produce disaccharides of type II from CSs, the polymer repeating units were conventionally represented as in II. Repeating units of KS were analogously drawn (Ia), with the hexosamine residue on the right. However, if the alternative disaccharide Ib is chosen instead of Ia, it is seen that the CS (Ii) and KS(Ib) disaccharides are both α-gluc, β-1,3-α-galact. The choice of either Ib or Ib (and their CS analogues) as repeating units is arbitrary. The recognition that both KS and CS are polylactoses, and that both polymers start with a complete ‘lactose’ unit at the reducing end, provides a formal basis for defining the repeating units of both KS and CS as ‘lactose’-based (III). The last (non-reducing) sugar in the linkage sequence is Gal (CS) or GaINAc or Man (KS) (III). The non-reducing terminal sugar in the last unit (I) of CS can be either Glc- or Gal-based, i.e. the last lactose unit need not be complete. The frequently used enzymes chondroitin lyases ABC and AC and keratan hydrolase I all cleave Gal–Glc bonds (III, arrowed). IV shows the gentle waves of the lines of the sugar rings in the plane of the KS polymer (above) and at right angles to the plane of the polymer (below, no substituents; only rings and glycosidic bonds are shown). The cross-hatched areas are hydrophobic groups; X = sulphate ester anionic groups, usually present on Glc C-6, and sometimes, but not necessarily, on Gal C-4. To scale. V, Scheme of proposed antiparallel CS:KS duplex, side view, with hydrophobic patches cross-hatched. Arrows point towards the reducing ends. The waveform present in the KS and CS backbones is shown to the left, in phase with that in both components of the duplex. Sugar rings are defined by dotted lines and labelled alongside. ○, ●. Acetamido groups; □, ■. Carboxylate groups.

Black symbols point out of the plane of the paper, and white symbols into the plane, respectively. Not to scale. NH → O—C—O H-bonds are possible between every pair of opposing disaccharides; hydrophobic patches overlap almost completely, and the shapes of the polymers shown as in IV (upper) are complementary.

Abbreviations used: CS, chondroitin sulphate; KS, keratan sulphate.
between CS and KS, their biosynthesis, enzymic degradation and evolution.

(1) The newly defined repeating unit (D-galacto β-1:4D-glucosamine) is D-lacto. KS is currently recognized as a polygalactosamine, but CS was not previously considered in this context. The recognition that CS and KS are both polysaccharides simplifies study of intermolecular interactions, since their shapes depend on identical backbones.

(2) The polymer backbone is the sequence (N-acetyl-D-glucosamine) in KS, and the linkage sequence is the first disaccharide unit (D-galacto β-1:4-D-glucosamine) in CS. In polysaccharides, the linkage sequences generally define the glycosidic bonds, and the linkage sites are determined by the structure of the glycosidic bonds. In both KS and CS, the linkage sequences are the first disaccharide unit, and the linkage sites are defined by the structure of the glycosidic bonds.

(3) The non-reducing end of the polysaccharide is defined by the first disaccharide unit, and the non-reducing end is the end opposite the reducing end. In KS, the non-reducing end is the end opposite the reducing end, and in CS, the non-reducing end is the end opposite the reducing end.

(4) The enzymes used to characterize KSs and CSs, keratanase hydrolases I and II, and chondroitin lyases AC and ABC, split the polysaccharide backbone at precisely the same points, the Gal-Glc bonds. Similarly, in KS, the first GlcNAc residue begins the polysaccharide chain, and the linkage sequence ends with a Man or GlcNAc residue.

(5) Lactose is found in mammalian milk. Apparently, it is not produced in other animal tissues or tissue fluids. The precise raison d'être of lactose in this context is a subject of speculation. Since lactose (but not CS or KS) is found in plants, the disaccharide may be evolutionarily more ancient than the polymer. It is biosynthesized by a simpler version (in that only one of the two sugars goes through a UDP stage) of the UDP-dependent pathways that produce CS and KS.

REFERENCES